

## Improved Incidence of Cardiovascular Disease in Patients with Incident Rheumatoid Arthritis in the 2000s: a Population-Based Cohort Study

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An excess burden of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) is well recognized, and many epidemiologic studies have reported up to 2-fold increased risk of incident CVD events and CVD mortality in RA compared to the general population. Earlier initiation of effective therapeutics for RA provides a premise for improved outcomes, including CVD outcomes. There is a signal from several population-based studies of improving CVD mortality after 2000. Decreased incidence of CVD events and decreased mortality after CVD events could both be contributors to the decreased CVD mortality in RA in recent years. However, longitudinal studies on trends in occurrence of CVD events and mortality after CVD events in patients with RA over time and studies comparing these trends between RA and the general population are scarce.

To address this gap in knowledge, we aimed to (1) assess trends in incidence of CVD in patients with incident RA in 1980–2009; (2) compare incidence of CVD in RA patients vs non-RA subjects with RA incidence/index date in 1980–2009; (3) assess mortality following incident CVD events in patients with RA in 1980–2009; and (4) compare mortality following incident CVD events in patients with RA vs non-RA subjects with RA incidence/index date in 1980–2009.

We studied Olmsted County, Minnesota residents with incident RA (age  $\geq 18$  years, 1987 ACR criteria met in 1980–2009) and non-RA subjects from the same source population with similar age, sex and calendar year of index. All subjects were followed until death, migration, or 12/31/2016. Incident CVD events included myocardial infarction and stroke. Patients with CVD before RA incidence/index date were excluded. Cox models were used to compare incident CVD events by decade, adjusting for age, sex, as well as for CVD risk factors and antirheumatic treatments.

The study included 905 patients with RA and 904 non-RA subjects.

Adjusting for age and sex, the risk of any CVD event in patients with RA in 2000s was 42% lower than in 1980s. The risk of MI was 56% lower in patients with RA in 2000s vs 1980s, while risk of stroke was similar in patients with RA across the decades. These results remained consistent after adjustment for age, sex, smoking, obesity, diabetes mellitus, hypertension, and dyslipidemia. The strength of association attenuated after adjustment for anti-rheumatic medication use, but the direction of association remained the same: HR 0.64, 95% CI 0.34–1.22. Trends including coronary revascularizations were similar to the trends for MI alone. Trends in incident CVD events and coronary revascularizations among rheumatoid factor (RF)-positive and RF-negative patients were similar to the RA cohort overall.

Unlike the over 50% excess risk of any CVD event in patients with RA in 1980s and 1990s, patients with incident RA in 2000s had no excess in any CVD events over non-RA subjects. Risk of death after a CVD event was somewhat lower in patients with RA after 1980s: HR: 0.54, 95% CI:0.33–0.90 in 1990s and HR: 0.68, 95% CI:0.33–1.41 in 2000s versus 1980s.

### Conclusion and take-home points:

- Incidence of major CVD events in RA has declined in recent decades. This improvement appears to be largely driven by an over 50% decline in the incidence of MI in patients with RA onset in 2000s versus 1980s, concomitant with the declining incidence of MI in the general population.
- The gap in CVD occurrence between RA patients and the general population is closing.
- Mortality after CVD events in RA may be improving.
- These findings highlight an important milestone in CVD disease management, likely reflecting improved CVD management in population overall, and RA-specific factors, such as improved control of systemic inflammation in RA following timely initiation of effective antirheumatic therapies.